**IN THE CLAIMS:** [amended claims for discussion only – clean set & marked set attached]

4. An active endoscopic device according to claim [2]3, wherein said diode lasers comprise lasers operating at different wavelengths.

10. An active endoscopic device according to claim 9, wherein [said]a homogenizing means is a partially reflective coating on said at least one balloon.

## REMARKS

Claim 8, which is objected to under 37 CFR 1.75, is cancelled.

Claim 4 has been amended to be properly dependant on claim 3, and claim 10 has been amended to remove the 35 USC 112 rejection.

As to claims 1 and 6, examiner contends that the present invention is anticipated by U.S. Pat. No. 5,468,238 by Mersch ('238). Patent '238 is described in the specification (page 2, lines 6-12) as follows:

"An endoscopic device which does place a radiation source at the distal end of the device, is demonstrated in U.S. Pat. No. 5,468,238. The referenced device places a single diode laser at the distal end to maintain spatial coherency and to reduce the loss of power; however, this device is limited in application. If applied for PDT purposes, a narrow light source makes the procedure slow and inefficient. The source of the light is limited to the single diode and therefore is limited to a single wavelength. Flexibility in the types of sources would create broader applicability for a device."

This patent describes an endoscopic device with a remotely powered radiation source located at the distal end of the endoscope. The laser beam produced by the diode is used to "both coagulate and cut tissue in an endoscopic procedure." (col. 1, lines 53-54) Patent '238 does not provide a means to create a diffuse radiation pattern, which is the primary focus of

the present invention. As described in claim 1 of the present invention, the radiation source "provides a diffuse radiation pattern across a section of body tissue". (emphasis added) Patent '238 only provides for a diode laser source at the distal end of the instrument. Furthermore, '238 appears to be primarily intended for use as a cutting or coagulating tool. Cutting and coagulating tissue requires a beam with a sufficient energy density to burn tissue, and would thus require a focused rather than a diffuse beam. All embodiments described in '238 focus the beam to a distinct point with the aid of focusing means such as a lens. A diffuse beam would render '238 useless for its disclosed purpose. A focused beam such as that disclosed in '238 would be ineffective for PDT treatments such as those contemplated by the present invention. Thus, because '238 does not provide for a diffuse radiation delivery pattern, it does not anticipate the present invention.

Examiner contends that claims 1-4 and 7-11 are anticipated by U.S. Patent No. 5,800,478 by Chen et al ('478). Applicant respectfully disagrees.

Patent '478 discloses an endoscopic apparatus and method for use in PDT comprising a flexible substrate positioned or positionable at the distal end of a probe for the application of electromagnetic or other energy. The flexible substrate can be delivered into the body and conform to areas or tumors with minimal invasion. Electronic microcircuits are positioned on the substrate to perform a variety of tasks such as photodetection or PDT. For PDT, light sources such as diodes or laser diodes are positioned on the substrate and surrounded by a flexible transparent envelope. Infrared power transmitted to an IR detector can be used to provide electric power from an external source to the substrate.

Patent '478 does disclose a plurality of diodes on the distal end of a probe, but fails to provide means for emitting a diffuse radiation pattern that is large compared to the probe or other substrate. Patent '478 relies on the shape of the substrate used to determine the radiation pattern, and thus requires that a special substrate be constructed for each body area. As described in patent '478, the "flexible substrate changes size and shape as necessary to maintain the light sources in close proximity with the treatment site". (col. 4, line 50) Producing a variety of differently shaped probes for different body areas can prove time

consuming and expensive. In contrast, the present invention provides for a radiation source emitting a large area diffuse radiation pattern that may be used for a more diverse range of treatments. With the present invention, a greater variety of treatment sites may be treated with one embodiment, because the emitted radiation pattern can effectively reach the treatment site without the need for close physical proximity. Although other sources beyond LEDs are disclosed, '478 apparently only contemplates use with light sources that have limited radiation patterns, because all the embodiments are meant to bring the light sources close to tissue. Thus, the present invention is distinct from '478 in that it utilizes a relatively large diffuse radiation pattern to reach tissue, rather than applying a device that conforms in shape and must be in close proximity to the treated tissue.

Patent '478 describes a number of embodiments, which are briefly described below to illustrate the need for close proximity between the probe and treated tissue, in contrast to the present invention. Figures 1-13 are described in the context of tumor irradiation wherein a tumor is pierced and the probe is guided into a tumor or other solid tissue mass. The light sources on the probe are in close proximity to the diseased tissue. Another example is shown in figures 14-16, wherein a plurality of flexible probes are splayed outward for treatment of the bladder. These probes, which may also take the form of loops, spread out so that the light sources are in close proximity to the bladder wall. The present invention contemplates irradiating a body cavity such as the bladder with a diffuse radiation pattern, obviating the need for such a complex and specialized device. Also disclosed by '478 are flexible sheet probes, which are folded prior to insertion and unfolded within the body, as is illustrated well in figures 17-21, which further demonstrate that '478 relies on physical proximity, rather than radiation pattern, to provide radiation to a treatment site. Figures 22-26 illustrate embodiments where the sheet probe is rolled prior to insertion and unrolled at the treatment site. Figures 29-35 show a cylindrical configuration of the flexible sheet probe. In this configuration, the sheet is constrained and inserted into a body lumen. The constraint is released, allowing the sheet to expand so as to physically contact the lumen wall. These embodiments can also be wrapped around a lumen to contact and treat exterior lumen walls. Figures 36-42 illustrate an embodiment where an esophageal or intestinal tumor is treated.

These embodiments, utilizing probes that may not come into full physical contact, nonetheless are limited to areas where a tumor is large enough to significantly narrow the passage to receive full radiation. Figures 43-45 illustrate further embodiments for arterial and cardiological use, which also appear to require insertion of the probe so that the light sources are in very close proximity to the treatment site.

The above descriptions demonstrate a significant difference between '478 and the present invention, namely that the probes discussed in '478 require physical contact or close proximity for the probes to be effective. This requires many separate designs for different treatment modalities. The present invention is not constrained in this manner, in that the probe described in the present invention provides a diffuse and relatively large radiation pattern that can effectively treat a variety of anatomical areas.

For the above reasons, the present invention is distinctly different from '478, and is thus not anticipated by '478.

Examiner contends that that the present invention is unpatentable over U.S. Patent No. 5,800,478 by Chen et al ('478) in view of U.S. Patent No. 6,254,594 B1 by Berry ('594). Applicant respectfully disagrees, in that it would not have been obvious to one skilled in the art at the time of the present invention to modify the system of '478 with the light source described in '594.

Patent '594 contemplates the use of a chemically luminescent mixture for the treatment of skin layers and for ophthalmic applications. It is meant to stimulate the release of factors to promote younger looking skin and to heat and reshape corneal tissue. It nowhere discloses a method for treating cancer or similar diseases. All disclosed embodiments describe the application of radiation from an external location to treat epidermal or corneal tissue. There is no indication that this may be an effective source for use in internal applications. The use of sample cells would appear to be unworkable with '478, in that in some cases the cell is activated by electromagnetic radiation. This would appear to be unsuitable for use as a light source on the substrate in '478, in that the light sources in '478 are powered by electric leads. Directly activating light sources in '478 with electromagnetic

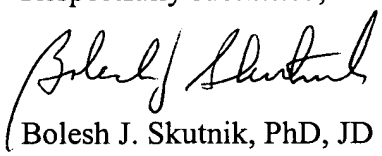
radiation is not contemplated. Additionally, the radiation produced for '594 is contemplated for producing heat in irradiated tissue, as opposed to '478, which provides radiation primarily for PDT. There is no indication that the chemically produced radiation in '594 would be useful in PDT applications.

Also, the chemiluminescent source described in the present invention is quite different from both the diode array in '478 and the chemical source in '594. The radiation source in '594 requires an electromagnetic or electric input to activate the luminescent qualities of the chemical mixture. The present invention discloses an embodiment wherein two chemicals are contained in a double walled balloon and mixed at the treatment site. Therefore, unlike both '478 and '594, the present invention requires no outside input of energy to activate the radiation source. Combining '478 and '594 would produce a device or system that is vastly different from the present invention.

Because there is no suggestion that a chemiluminescent cell such as that described in '594 would be of any use as a light source on a flexible substrate as in '478, it would not be obvious to combine the two inventions. Furthermore, combination of the two inventions would not anticipate the present invention, in that the present invention and '478 are distinctly different, as described earlier. Therefore, the present invention is not obvious.

With these changes and remarks, it is believed that the disclosure is now in condition for allowance. Reconsideration is respectfully requested. An early and favorable response is earnestly solicited. Thank you.

Respectfully submitted,



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**What is claimed is:**

1. An active endoscopic PhotoDynamic Therapy (PDT) comprising:

A distal and a proximal end;

A radiation source positioned at said distal end;

Wherein said source provides a diffuse radiation pattern across a section of body tissue, which is large compared to said endoscopic device's distal cross section, and which is in proximity to said distal end; and

Wherein said radiation source is powered remotely and operates at a pre-selected wavelength and power range compatible with requirements of a selected PDT drug.

2. An active endoscopic device according to claim 1, wherein said radiation source is a multitude of diodes mounted on said device's distal end so as to create an illumination pattern to effectively irradiate a selected treatment site.

3. An active endoscopic device according to claim 2, wherein said diodes are diode lasers.

4. An active endoscopic device according to claim [2]3, wherein said diode lasers comprise lasers operating at different wavelengths.

5. An active endoscopic device according to claim 1, wherein said radiation source is provided by chemiluminescence.

6. An active endoscopic device according to claim 1, further comprising cooling means.

7. An active endoscopic device according to claim 1, further comprising means to deliver a substance which will be activated by said radiation.

[8. An active endoscopic device according to claim 1, further comprising means to deliver a substance which will be activated by said radiation.]

9. An active endoscopic device according to claim 1, further comprising at least on balloon to serve as a centering mechanism.

10. An active endoscopic device according to claim 9, wherein [said]a homogenizing means is a partially reflective coating on said at least one balloon.

11. A method of performing PhotoDynamic Therapy with an active endoscopic device such as in claim 1, comprising the steps of:

(a) positioning a catheter/endoscope into a patient and directing it to a predetermined treatment site within said patient.

(b) Placing said active endoscopic device into said endoscope/catheter and advancing it so that its distal end with its radiation source are at a distal end of said endoscope; and

(c) Energizing said radiation source and irradiating said selected treatment site for times and periods to achieve said PDT treatment for said selected treatment sites.

## Abstract of the Disclosure

[Briefly stated the present invention provides an] An active endoscopic system is disclosed [which contains] containing an electromagnetic radiation system located at the distal end of the endoscopic device allowing for variable intensity application of desired wavelengths in the application of PhotoDynamic Therapy (PDT) over a broad area. The power sources are varied according to the needs of a specific application. Various attachments and configurations may be used [in conjunction with the endoscopic device] to enhance performance of a desired application[. Such enhancements may include], including but [are] not limited to multi–balloon systems for centering the apparatus or limiting the treatment area, fiber optics for directly viewing the treatment area [of treatment], vacuum systems for [the] waste removal [of waste product], [delivery] tubes for [the delivery of] delivering aminolevulinic acid (ALA) or other photosensitizers, and other fiber optics for illumination of treatment area. A preferred embodiment [of this system] for [use in] PDT employs a multitude of low wattage diodes at the distal end of the endoscope, a scattering glass, cooling channel, external cooling unit, an inflatable balloon with a reflective surface[,] and a tube connected to an external pump for the delivery and removal of photosensitizers. Each diode is selected to emit the respective frequency needed to activate the selected photosensitizer. Alternatively, a range of diodes may be selected to maximize the activation of the photosensitizer. Other embodiments include a chemiluminescent light source at the distal end of the endoscope. [double walled balloon fed through a channel of an endoscope which would allow mixing of chemiluminescent chemicals as an alternative light source within the channel between the balloons. Still other embodiments include different] Other electromagnetic sources [for the emission of] include microwave[s] or radio frequency devices. The prime benefit of this [invention] system is the placement of the [electromagnetic] radiation source at the distal end of the device to bring the light source directly to the desired site.